

Retroperitoneal Subpancreatic Ectopic Pregnancy Following In Vitro Fertilization in a Patient with Previous Bilateral Salpingectomy: How Did It Get There?

W. P. Dmowski,^{1,2,4} N. Rana,^{1,2} J. Ding,¹ and W. T. Wu³

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An unusual case of retroperitoneal ectopic pregnancy is reported. The patient, a 34 year old nulligravida, underwent IVF/ET following bilateral salpingectomy. A small, degenerating, intrauterine gestational sac suggested failing intrauterine pregnancy. There was no intraperitoneal free fluid. On Day 41 after ET, the patient was hospitalized because of acute epigastric pains. A pseudocyst of the head of pancreas was demonstrated by CT scan. A day later, exploratory laparotomy, because of a precipitous drop in the hemoglobin, revealed a massive retroperitoneal hematoma and an embryo in the gestational sac attached to the head of pancreas and major blood vessels. The patient did well following surgery. The mechanisms of retroperitoneal embryo migration are discussed and literature is reviewed.

KEY WORDS: Ectopic pregnancy; IVF; bilateral salpingectomy; retroperitoneal upper abdominal pregnancy.

INTRODUCTION

The prevalence of ectopic pregnancies following Assisted Reproductive Techniques (ART) is about eight times higher than in the general population and accounts for approximately 5% of all ART pregnancies (1). The majority of these are tubal, although cornual, cervical, broad ligament, ovarian, primary abdominal, and heterotopic abdominal pregnancies have also been reported. It has been suggested that extrauterine embryo implantation during ART cycles is related to the embryo transfer (ET) technique and that tubal disease is a major risk factor (2,3). Transuterine intratubal placement of the embryos may be the cause of some tubal pregnancies but it is much more

difficult to explain the mechanism of upper abdominal retroperitoneal embryo implantation following in vitro fertilization (IVF)/ET. Retroperitoneal ectopic pregnancies are difficult to detect and may be associated with the massive retroperitoneal bleeding. Only one such case has been reported previously (4). Our case is the first report on a retroperitoneal upper abdominal pregnancy mimicking a pseudocyst of the head of pancreas following IVF/ET in a patient with prior bilateral salpingectomy.

CASE REPORT

The patient was a 34-year-old nulligravida with primary infertility of 4 years duration and bilateral hydrosalpinx diagnosed laparoscopically. Two IVF/ET attempts and two additional ETs with cryopreserved-thawed embryos were unsuccessful in spite of good quality embryos. Endometrial integrin studies demonstrated normal expression of AV β 3 integrins. It was assumed that hydrosalpinx was the factor preventing intrauterine embryo implantation, and

¹ Institute for the Study and Treatment of Endometriosis, Oak Brook, Illinois 60523.

² Rush Medical College, Chicago, Illinois 60612.

³ Private practice, Westmont, Illinois 60559.

⁴ To whom correspondence should be addressed at Institute for the Study and Treatment of Endometriosis, 2425 West 22nd Street, Suite 102, Oak Brook, Illinois 60523.

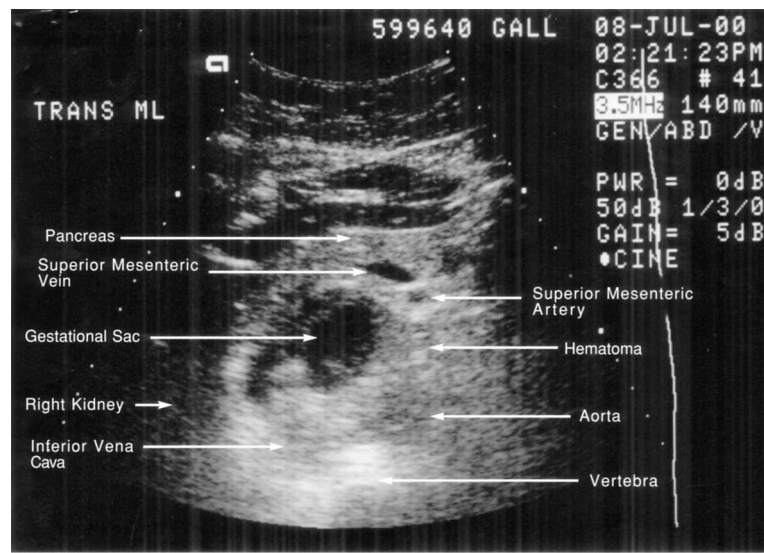


Fig. 1. Transverse scan of the upper abdomen showing the gestational sac adjacent to the head of pancreas.

bilateral laparoscopic salpingectomy was performed. The clinical diagnosis of hydrosalpinx was confirmed histologically. Three months after salpingectomy, another IVF/ET procedure was performed. For this purpose, midluteal GnRH-a pituitary down regulation was followed by controlled ovarian hyperstimulation using recombinant FSH according to a standard protocol. When 10 follicles were between 14 and 23 mm in diameter and estradiol level was 2498 pg/mL, hCG 10,000 IU was administered. The uterus was anteverted and during the preceding cycle was sounded to 8.3 cm without difficulty. Fifteen oocytes were retrieved transvaginally, 14 fertilized, and three 8–12 cell embryos were transferred on Day 3 after retrieval with the use of Edwards–Wallace Embryo Transfer Catheter (Sims Portex, Hythe, Kent, UK). The procedure was atraumatic and was performed in the Trendelenburg's position. The tenaculum was not used and the transfer was monitored in its entirety with transabdominal ultrasound. The embryos were transferred in a total of 40 μ L of culture medium (G2.2 Scandinavian IVF Science AB) and intracavitary placement of the embryos was clearly demonstrated ultrasonographically. Before, ET assisted hatching was performed as described previously (5). Following ET, the patient remained in the supine position for 2 h and received standard luteal support consisting of progesterone in oil 100 mg daily. Serum beta hCG levels were 124 mIU/mL on Day 12 after ET, 595 mIU/mL on Day 15, 4594 mIU/mL on Day 22, and subsequently increased

exponentially to 38,635 mIU/mL on Day 40 after ET. Transvaginal ultrasound on Day 22 after ET demonstrated a small intrauterine gestational sac measuring 2.1 \times 2.8 mm. The sac failed to develop further and high resolution level III ultrasound was unable to detect the yolk sac or embryonic development. Failing intrauterine pregnancy was diagnosed and the luteal support was discontinued 40 days after ET. There was no evidence of intraperitoneal free fluid on any of the pelvic sonograms performed during that period. A day later, the patient experienced a sudden onset of right epigastric and right upper back pains and weakness. She was taken by ambulance to a local hospital where abdominal and pelvic ultrasound examinations were performed. Again there was no free fluid in the pelvis or abdomen. In the upper abdomen, a pseudocyst of the head of pancreas measuring 2 \times 3 cm was described, situated immediately beneath and below the head of the pancreas (Fig. 1). During the night at the hospital, the patient became hypotensive and restless and abdominal pain increased in intensity. The hemoglobin and hematocrit levels decreased from 13.2 g/dL and 38.9% respectively on admission, to 7.9 g/dL and 23.1% the following morning, and the patient was brought to the operating room for emergency laparotomy. At laparotomy, a large retroperitoneal hematoma was noted. It extended from the subhepatic space along the ascending colon, transverse colon, around the right kidney to the inferior portion of the Gerota's fascia, across the midline vessels, and further under the head of

pancreas. The hematoma was evacuated and a cystic structure posterior to the duodenum and attached to the head of pancreas, vena cava, as well as mesenteric and portal veins, was identified and removed. Grossly, products of conception with placenta were noted and histologically, embryo with gestational sac and chorionic villi were identified. The patient had a blood transfusion during surgery but her postoperative course was uneventful and she was discharged home on the fifth postoperative day with falling serum Beta hCG levels.

DISCUSSION

It is not surprising that the prevalence of ectopic pregnancies is higher following ART procedures than in the general population. Tubal as well as peritubal disease are the major indications for ART and both have been considered as a major risk factor for the ectopic pregnancy (3). The mechanism of tubal pregnancies in such cases can involve either a direct placement of the embryos in the diseased fallopian tube or a migration of the embryos into the fallopian tube subsequent to the uterine placement. It has been suggested that the technique of embryo transfer, namely high insertion of the embryo transfer catheter (more than 60 mm from the external os), or high volume (more than 50 μ L) of the embryo transfer media may increase the risk (2). Hydrosalpingeal fluid accumulated in the diseased fallopian tubes has been shown in vitro to have an embryo-toxic effect, and women with hysterosalpinges seem to have lower success rates with ART procedures (6). For this reason, salpingectomy or tubal occlusion in the interstitial portion of the tube have been recommended to prevent tubal pregnancies and to improve chances for uterine implantation (7). This trend has been followed by reports of ectopic pregnancies in unusual sites in women with previous salpingectomies (4,8,9).

Primary abdominal pregnancy is a rare and potentially fatal variant of the ectopic pregnancy (10). Its prevalence seems to be also higher following ART procedures than in the general population (9). Several such cases have been described following unilateral or bilateral salpingectomy raising the possibility of intraabdominal placement of the embryos during the transfer procedure (4,9). However, abdominal pregnancy in the retroperitoneal space is an exceedingly rare occurrence and only one such case following an ART procedure has been reported previously

(4). Similarities between that case and our present report warrant further discussion. Both patients were admitted to the hospital during the 7th week of the IVF/ET cycle because of an acute onset of right abdominal pains in the previous case, and epigastric and upper back pains in our patient. Both patients had highly elevated Beta hCG levels and either no gestational sac in the uterus, as in the prior report, or a small degenerating intrauterine gestational sac, as in our patient, suggesting a progressing ectopic pregnancy. Yet in both cases, there was no free intraperitoneal fluid indicative of intraperitoneal bleeding.

Abdominal ultrasound in the previous case demonstrated on a transverse scan a suspected gestational sac in the retroperitoneal space in the mid abdomen and in our patient, a retroperitoneal cystic structure suggestive of a pseudocyst of the head of pancreas. In both patients, there was a precipitous drop in the hemoglobin and hematocrit levels while in the hospital and in both patients, exploratory laparotomy demonstrated massive retroperitoneal hematoma. A retroperitoneal gestational sac was identified in the mid abdomen in the prior report and in our case a gestational sac with the embryo was adherent to the duodenum, head of the pancreas, and major blood vessels. The outcome in both cases was satisfactory in spite of the massive retroperitoneal hematomas and the need for blood transfusions. Past medical history in the prior case included a right salpingectomy for tubal pregnancy and a left hydrosalpinx and in our patient, a bilateral salpingectomy for hydrosalpinges.

It is quite likely that some retroperitoneal bleeding and a beginning of the retroperitoneal hematoma formation were present in both patients at the time of hospital admission and were responsible for the acute onset of abdominal pains. With prompt hospitalization, further drop in the hemoglobin levels secondary to the massive retroperitoneal bleeding occurred in the hospital and immediate life-saving laparotomy could be performed expediently. In this context, the importance of the careful follow up of all ART pregnancies until the site of implantation is well established cannot be overemphasized.

The most unusual and difficult to explain in both cases is the site of the ectopic implantation. The iatrogenic placement of the embryos in the retroperitoneal space of the mid or upper abdomen can definitely be excluded considering the length of the transfer catheter and the volume of the embryo transfer medium. The possibility of intraabdominal

placement of the embryos and subsequent spontaneous migration to the retroperitoneal space without any indication of the peritoneal injury also seems unlikely. The only possibility that remains is a spontaneous migration of the embryos from the uterine cavity to the site of the final implantation.

In our patient, the entire process of embryo transfer was atraumatic and was continuously monitored sonographically. Intracavitary placement of the embryos was clearly demonstrated and was further indicated by the likely intrauterine implantation of one of the embryos. The mechanism of the second embryo migration to the retroperitoneal space of the upper abdomen is the most puzzling. It seems quite obvious that this migration could not have been direct but must have followed the vascular or lymphatic channels. Dissemination of the cells or tissue fragments through the vascular channels, as in the case of trophoblastic diseases, typically terminates in the pulmonary tissue (11). However, dissemination of the endometrial cancers through the lymphatic channels leads to the metastases in the periaortic and portal hepatic nodes (12). Considering the site of both ectopic gestations, the route of embryo migration from the uterus to the retroperitoneal space in our patient and in the previous case (4) must have involved the lymphatic channels.

In summary, we have presented here an unusual case of upper abdominal retroperitoneal ectopic pregnancy following IVF/ET in a patient with previous bilateral salpingectomy. Only one similar case was reported previously. A review of the literature demonstrates an increased frequency of ectopic pregnancies following ART procedures with a tendency to unusual sites of embryo implantation in women with prior salpingectomies. The mechanism of embryo migration following intrauterine placement appears to be most likely through the lymphatic channels.

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