Isotretinoin (Ro-Accutane) teratogenesis. A case report

C.H. Giannoulis, K. Papathanasiou, T.H. Tantanasis, V. Vaitsi, I. Tzafettas

2nd Department of Obstetrics and Gynecology, Aristotle University, Thessaloniki (Greece)

Summary

A case of teratogenesis in a 16-year-old pregnant patient is described. She had been using 60 mg Ro-Accutane daily till the 16th week of gestation. Sonography showed no cephalic skull up to the frontal bone of the fetus. A central lagostroma was also detected.

Key words: Isotretinoin; Teratogenesis; Sonography.

Introduction

Retinoids are basic ingredients for the preparation of synthetic vitamin A and are widely used for acme therapy. One of the most extensively used drugs is Ro-Accutane, containing isotretinoin [1]. The prescription of this drug during pregnancy can cause serious malformations to the embryo. The main embryopathies are noticed at the exterior ear, the skull, and the brain. The teratogenetic effect of isotretinoin is so strong that pregnancies occurring shortly after therapy completion usually end in spontaneous abortion [2].

Case Report

Our patient was examined as an outpatient in the 2nd Department of Obstetrics and Gynecology on January 17, 2003 for the first time during the 27th week of pregnancy. She was a 16-year-old, unmarried primigravida, and she had not been examined before. Her personal and family history were unremarkable. However she had been using 60 mg Ro-Accutane daily till the 16th week of her gestation.

After routine exams the patient underwent sonography during which a single embryo with positive cardiac function but serious malformations was confirmed. The placenta was normal, graded OO, and the amniotic fluid was increased. There was no cephalic skull up to the frontal bone, and depiction of the spinal column was not clear. There was no stomach seen, and a central lagostroma (lagentonum) was detected. Fetal measurements showed that the embryo was two weeks in growth retardation. Amniocentesis followed confirming a normal karyotype.

Labor was inducted using prostaglandins and the patient left the hospital three days later in good condition. Macroscopic examination of the neonate confirmed the sonographic findings. The biopsy showed esophagus atresia and small interventricular cardiac foramen.

Discussion

As referred our patient used the teratogenic drug for a long period before and till the 16th week of her pregnancy for acme therapy. Additionally isotretinoin (Ro-Accutane), retinol, etretinate and tretinoin cause the same toxic effects [3]. It has also been noted that although the toxic effects are similar for all four derivatives, the importance and the location of the damage varies depending on the duration the drugs were used [4]. The drug usually effects the midbrain and the cerebellum vermis, according to experiments on macaque apes with similar brain anatomy [5]. In accordance with various researches, the toxic effect of retinoids to the fetal hypothalamus is responsible for growth retardation. The damage caused in this specific area of the brain is considered to be responsible for the secretion of A-MSH hormone which stimulates embryo growth. It seems that damage in the same area causes malformations of the spinal columm [6].

It is worth mentioning that these embryos can become organ donors considering the fact that a sufficient number of organs are healthy, although of less immunological reaction, and that receivers are children [7].

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Address reprint requests to:
V. VAITSI, M.D.
2nd Dept. of Obstetrics and Gynecology
Aristotle University of Thessaloniki
Hippokratio General Hospital
Kostantinoupoleo 49, P.O. Box 54642
Thessaloniki (Greece)

Ectopic missed abortion after laparoscopic sterilization with the harmonic scalpel

N. Dalkalitsis, S. Stefos, P. Tsirkas, G. Tsanadis, A. Sotiriadis, V. Dousias

Division of Endoscopic Surgery, Department of Obstetrics & Gynecology, University Hospital of Ioannina (Greece)

Summary

A case of a patient who presented with ectopic pregnancy and subsequent missed abortion one year after laparoscopic sterilization with the harmonic scalpel is reported. According to our knowledge of the relevant literature, this is the first time that a case of ectopic pregnancy after sterilization with a harmonic scalpel has been reported.

Key words: Harmonic scalpel; Ultracision; Ectopic pregnancy; Tubal sterilization.

Introduction

Laparoscopic sterilization of the fallopian tubes is a quite common, safe and efficacious method for contraception. The failure rate of this method reached 7.3‰ after ten years follow-up [1]. This method is superior to the tubal ring application, where the pregnancy rate after sterilization is 36.5‰ [2]. The majority of those pregnancies were ectopic, reaching a percentage up to 76% [3, 4].

We report the first case, according to our knowledge of the relevant literature, of a patient admitted to our department because of ectopic pregnancy that ended up as a missed abortion one year after a laparoscopic tubal dissection with a harmonic scalpel.

Case Report

A 34-year-old female presented to the outpatient clinic of Ioannina University Hospital complaining of vaginal bleeding, deep lower abdominal pain and secondary amenorrhoea of two months' duration. Her past medical history included two normal vaginal deliveries, one miscarriage and four selective terminations of pregnancy. There was no history of abdominal surgery. She had also undergone laparoscopic sterilization of both tubes with the harmonic scalpel a year before. There were no pre- or postoperative complications at the time of the laparoscopic sterilization.

After her admission to our department the physical examination revealed vaginal bleeding, a slightly enlarged uterus of soft consistency and increased sensitivity during deep bimanual palpation of the right adnexal area. The patient's vital signs were normal. Transvaginal ultrasound findings were: uterus 53 x 59 mm in size, endometrial thickness 11 mm, no gestational sac seen in the uterine cavity, both adnexae normal and a small amount of fluid was identified in the pouch of Douglas. The pregnancy test was positive and the β-HCG level was 206 IU/l. The patient was admitted to the Gynecology Department. The β-HCG levels increased from 303 to 324 IU/l over two days' time. The patient's symptoms were persistent and her condition was deteriorating. The provisional diagnosis was ectopic pregnancy and a diagnostic laparoscopy was performed.

Laparoscopy revealed a slightly enlarged uterus, with no obvious fibroid changes. Both ovaries looked normal. The right fallopian tube was dissected at the ampulla and the distal end was found slightly enlarged and slightly bleeding due to an ectopic missed abortion sited at the distal tubal end (Figure 1). The left fallopian tube and its mesosalpingeum had the expected appearance of a previous dissection at the isthmus area, due to previous laparoscopic sterilization (Figure 2). A small quantity of blood, approximately 20 ml, was retrieved from the pouch of Douglas. There were no adhesions either at the site of dissection of both the fallopian tubes or at the pelvis.

We proceeded by squeezing the distal part of the right tube with grasping forceps (milking out) and removed blood clots and hemorrhagic tissues. Methylene blue infusion with a Fickenser uterine manipulator did not fill either proximal end of the tubes and no leakage of dye was noted in the abdominal cavity. After that, we performed repeat tubal resection using a harmonic scalpel in level 3. We secured hemostasis in this particular tissue area and 2 cm proximal tubal length was left. Diagnostic curretage was performed simultaneously. Pathological examination of the endometrial tissue demonstrated residual reaction of the endometrium and absence of chorionic villi. The patient remained in the hospital for two days postoperatively without complications, while her β-HCG level declined to 41 IU/l. She was discharged on day 3 postoperatively and had no further problems.

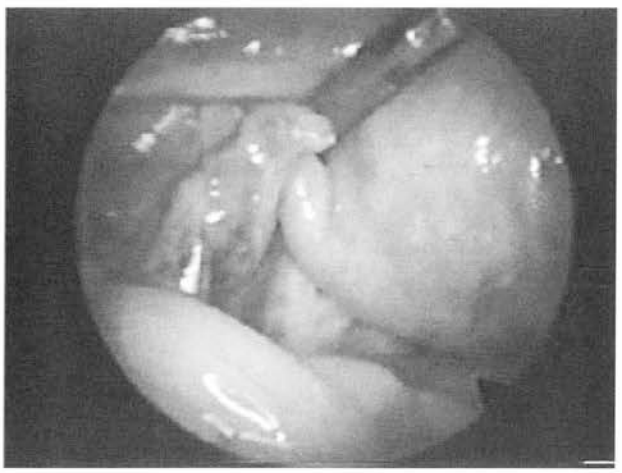

Figure 1. — Left fallopian tube with missed abortion at the distal end.

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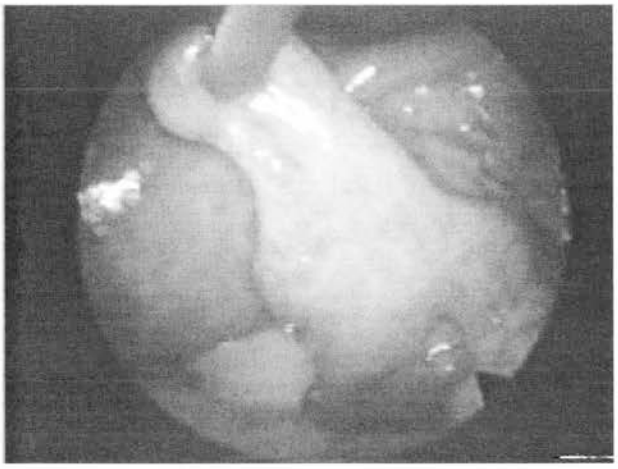

Figure 2. — Right fallopian tube with previous laparoscopic sterilization.

Discussion

The subsequent pregnancy rate after laparoscopic sterilization differs and it seems to be associated with the applied technique and the patient's age [1]. The risk of pregnancy after ring clip application varies by location of clip application, history of tubal disease and history of abdominal or pelvic surgery. The rate of pregnancy ranges from 7.1 per 1,000 procedures to 78.0 per 1,000 procedures in a period of ten years [5]. Tubal electrocautery with diathermy seems superior than the applied tubal ring and the pregnancy rate is significantly lower, 7.5/1,000 vs 36.5/1,000 procedures at five years. The majority of cases (76%) were ectopic pregnancies.

During a five-year period, 57 laparoscopic sterilizations were performed in our department using a harmonic scalpel [6]. No complications such as tubal bleeding or abdominal pain occurred. The mean operative time was seven minutes.

We believe that use of a harmonic scalpel has distinct advantages compared to other laparoscopic sterilization methods. Laparoscopic sterilization with a harmonic scalpel causes less thermal damage and less charring of the tissues, resulting in minimal ischemia, therefore reducing the risk of postoperative formation of adhesions and resulting in better healing. Reduced thermal damage of tissues produces less smoke and tissue debris and results in better visualization, which minimizes operative time [7]. The harmonic scalpel provides effective coagulation and cutting at the same time, so there is no incidence of tubal bleeding during the procedure, which also results in shorter operative time.

These features of the harmonic scalpel render it safe and easy to use for laparoscopic sterilization [8]. Although the number of cases is small, the definite absence of complications and the shorter operative time support this view. To the extent of our knowledge, this is the first time that a case of ectopic pregnancy after sterilization by harmonic scalpel has been reported.

We conclude that, despite the very low pregnancy rate after laparoscopic sterilization, the procedure does not completely eliminate the possibility of ectopic pregnancy, even years after the operation. Patients should be counseled appropriately, especially younger sexually active women, and they should be informed of the very low, however existing, risk of ectopic pregnancy in the following years.

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Address reprint requests to:
T. STEFOS, M.D.
Associate Professor of Ob.-Gyn.
N. Papadopoulou 3
45444 Ioannina (Greece)