

CASE REPORT

Pregnancy After Tubal Sterilization in a Woman Treated with Biologics for Severe Psoriasis

Charlée Nardin · Morgane Colas · Vincent Curie · Fabien Pelletier ·
Eve Puzenat · François Aubin 

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ABSTRACT

Little is known about whether immunosuppressed patients mount the immunological response necessary to ensure tubal occlusion. Theoretical concern for non-occlusion has limited the use of hysteroscopic sterilization in patients on immunosuppressive therapies. The effects of tumor necrosis factor-alpha (TNF- α) blockers and interleukin (IL)-17 inhibitors on contraception and pregnancy for patients with psoriasis are poorly documented. We report a case of pregnancy that ended in miscarriage in a patient treated first with TNF- α and then with IL-17 inhibitors for severe psoriasis after tubal sterilization with micro-inserts. Our observation suggests that the efficacy of tubal sterilization by micro-inserts may be impaired by these two biologics and that the risk of miscarriage may be

increased in women with psoriasis treated with secukinumab.

Keywords: Biologics; Pregnancy; Psoriasis; Sterilization

INTRODUCTION

Micro-inserts are a non-incisional permanent method of contraception. The micro-insert is a dynamically expanding micro-coil. When the micro-inserts are in place, body tissue grows in them and blocks the fallopian tubes, resulting in permanent contraception. The effects of both tumor necrosis factor-alpha (TNF- α) blockers and interleukin-17 (IL17) inhibitors on contraception and pregnancy are poorly documented. We report a case of pregnancy that ended with miscarriage in a patient treated with these biologics for severe psoriasis after tubal sterilization with micro-inserts.

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C. Nardin · M. Colas · F. Pelletier · E. Puzenat ·
F. Aubin (✉)
Service de Dermatologie, Centre Hospitalier
Universitaire, Université de Franche Comté, Unité
de recherche EA 3181, Besançon, France
e-mail: francois.aubin@univ-fcomte.fr

V. Curie
Service de Gynécologie, Centre Hospitalier, Dole,
France

CASE REPORT

Informed consent was obtained from the patient for being included in the study.

A 45-year-old white female patient had suffered from cutaneous psoriasis since her adolescence. She had six children delivered vaginally and one miscarriage. At the age of

43 years, she underwent hysteroscopic tubal sterilization with micro-inserts (Essure®; Conceptus Inc., Bayer AG, Leverkusen, Germany). At age 40 years, she developed severe psoriasis involving 30% of the body surface area that had a major impact on her quality of life. The psoriasis had been successively treated with methotrexate, TNF inhibitors (etanercept, adalimumab, infliximab from age 40 to 44 years) and lastly secukinumab. After 3 months of treatment with secukinumab, she developed amenorrhea. Measurements of human chorionic gonadotropin levels and an ultrasound scan revealed interruption of an intra-uterine pregnancy at 6 weeks of gestation. She was treated by dilatation and curettage.

DISCUSSION

Contraception is recommended for women who are treated with biologics for psoriasis. Although a few cases of successful hysteroscopic sterilizations with micro-inserts in patients treated with steroids, mycophenolate mophetil and sirolimus have been reported, this method of contraception in immunosuppressed women is discouraged by the manufacturer [1]. Currently, the instructions for use included in each Essure® kit contain the following warning: “Patients undergoing immunosuppressive therapy are discouraged from undergoing the Essure® procedure because the immunosuppressant may lead to decreased tissue ingrowth” [2]. It should be noted that this sterilization implant was recently withdrawn from the non-USA market because of different adverse events, including chronic pain, perforation of the uterus and fallopian tubes. Our case report highlights that the efficacy of tubal sterilization with micro-inserts may be impaired by treatment with TNF inhibitors as well as IL-17 inhibitors. Histologically, the micro-inserts produce an immediate foreign body inflammatory reaction at 2–3 weeks followed by fibrosis at between 8 and 30 weeks [3]. Because foreign body cells participate in the inflammatory response through the production of cytokines, including TNF- α and IL-17 [4], their inhibition could theoretically alter the foreign body

reaction. Continuing to use another form of contraception during a 3-month period until bilateral tubal occlusion is documented by hysterosalpingogram or ultrasound is thus recommended in all immunosuppressed patients who undergo hysteroscopic sterilization [1].

Our case also suggests that TNF blockers and secukinumab may also be involved in the occurrence of spontaneous abortion. It has been hypothesized that anti-TNF treatment at the time of conception may be associated with an increased risk of spontaneous abortion [5]. However, the role of anti-TNF- α agents on spontaneous abortion in this case is unlikely since the patient had stopped taking anti-TNF- α agents for many months when she inadvertently became pregnant.

It should also be noted that the patient’s profile fulfilled three risk factors for spontaneous abortion: she had had one spontaneous abortion, she was 45 years old and she was multiparous [6–8]. Thus, the possibility cannot be excluded that this spontaneous abortion fell into the rate of abortions (25%) taking place in the general population [9].

It has been reported that patients suffering from psoriasis have an increased rate of pregnancy complications, such as spontaneous abortions, recurrent pregnancy losses, failure to conceive and preterm deliveries [10, 11], although reports on pregnancy outcomes in women with psoriasis are conflicting [12, 13]. A recent review suggested that immune system deregulation in psoriasis likely leads to poorer outcomes in pregnancy [14].

Our case is the first report of pregnancy in a patient on secukinumab therapy. Regarding IL17-inhibitors, developmental toxicity studies in animals found that the administration of secukinumab during pregnancy in cynomolgus monkeys did not result in maternal toxicity, embryofetal toxicity or teratogenicity [15]. To date, controlled data in human pregnancy are not available. Thus, it is possible that IL-17 inhibitors are toxic to the human embryo even if toxicity studies in animals have not yet demonstrated it. A balance between T helper 1 (Th1), T helper 17 (Th17) and T helper 2 (Th2) signaling pathways is indeed required for implantation, development of the placenta and

maintenance of pregnancy [16]. Thus, it could be hypothesized that IL-17 inhibitors may compromise the immunity of the fetus and neonate by dysregulation of the Th17 balance.

On the other hand, it is hypothesized that pro-inflammatory cytokines which are elevated in the sera and psoriatic skin have detrimental effects on the maternal placenta and could thus lead to adverse pregnancy outcomes. During pregnancy, the foreign fetal antigens challenge the maternal immune system, and Treg cells will dominate Th17 cells to guarantee fetal survival. An increased Th17/Treg ratio has been found in patients with pregnancy complications and autoimmune diseases [16]. These data suggest that human Th17 cells may play a major role in rejecting conceptus antigens and that restoration of Th17 balance with IL-17 inhibitors might protect these patients from pregnancy loss [16]. However, such data have not been obtained from psoriasis patients and therefore no conclusion can be drawn for this population.

CONCLUSIONS

In conclusion, the failure of sterilization and subsequent spontaneous abortion in a biologic-treated patient is likely simply a coincidence. However, we cannot exclude the possible role played by the biologics. A better understanding of the role of the TNF- α and IL-17 signaling pathways in the inflammation reaction of the fallopian tubes induced by micro-inserts, in pregnancy maintenance and in miscarriage may help to define recommendations for contraception and pregnancy in women with severe psoriasis treated with TNF- α and IL-17 inhibitors.

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Compliance with Ethics Guidelines. Informed consent was obtained from the patient for being included in the study.

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