Ectopic pregnancy with Implanon®

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**Case report**

A 25-year-old, non-smoking woman, para 2+0, presented at our family planning clinic complaining of having experienced intermittent pelvic pain over the previous 2 weeks. She reported 7 weeks of amenorrhoea, of feeling pregnant, and stated that two home pregnancy tests had tested positive. She had had an Implanon® inserted 28 months previously and this was easily palpable at the clinic. A pregnancy test done in the clinic was negative. The patient wished to have her implant removed and arrangements were made for this to be done 9 days later. The patient re-presented the following day having done two further home pregnancy tests that were positive. A repeat pregnancy test done in the clinic subsequently gave a positive result. An ultrasound scan was carried out but no intrauterine echo was detected. Blood was then taken to measure the beta human chorionic gonadotropin (β-hCG) level and this was repeated 2 days later. The β-hCG levels in both samples were raised and the patient was immediately referred for laparoscopy. At surgery, a distended right Fallopian tube was found and subsequent microscopy confirmed a right tubal ectopic pregnancy.

One week later the patient attended for follow-up. Arrangements were made, in conjunction with Organon (Implanon’s manufacturer), to have blood taken for serum etonogestrel assay. This involved attendance at the local biochemistry laboratory where 10 ml blood was taken, processed and transported by courier under dry ice conditions to the Organon laboratories in The Netherlands. The patient was given condoms to use in the interim as any hormonal contraception could have affected future assays. Once the blood had been taken the patient returned for removal of the implant. This was also dispatched to Organon in The Netherlands where it was to be tested for its integrity and residual hormone content should the blood levels of etonogestrel be found to be within the expected range. The plasma level of etonogestrel was 105 pg/ml and the daily release rate and residual content were within the range expected given the length of time the implant had been in situ. The woman’s body mass index was 26 (height 1.68 m, weight 69 kg). She had no history of pelvic inflammatory disease. She had undergone a laparoscopy several years previously to investigate abdominal pain, however no abnormality was found. A chlamydial screen done at that time was negative. The patient’s two subsequent pregnancies had been conceived easily and had resulted in normal vaginal deliveries. Previous contraception had consisted of Depo-Provera® prior to the woman’s first pregnancy and the progestogen-only pill between pregnancies and immediately following her second pregnancy. Her only medication had been the selective serotonin re-uptake inhibitor, sertraline, 100 mg daily taken for an 18-month period up until approximately 2 months prior to her presentation. She had regular periods during the 2 years in which Implanon had been in situ.

**Discussion**

Implanon is a subdermal implant comprising an ethylene vinyl acetate copolymer cylinder with a core containing 68 mg etonogestrel, the biologically active metabolite of desogestrel, a progestogen widely used in oral contraceptives. Clinical trials performed during the implant’s development reported no pregnancies. In 1998, data were available for 4103 woman-years (in excess of 53 000 treatment cycles) giving a Pearl index of 0.0. Implanon was introduced in Europe in 1998 and in the UK in October 1999. Experience of Implanon’s use since then has produced some unintended pregnancies, although in many of these cases the conceptions have occurred as a result of failures arising from non-insertion, prior conception, drug interaction with enzyme inducers, and so on, rather than due to primary failure of the contraceptive effect.

Implanon achieves its contraceptive effect by inhibition of ovulation and by effecting changes in the cervical mucus which hinders the passage of spermatozoa. The release rate of etonogestrel decreases with time so that by the end of the first year of use the mean concentration of etonogestrel is 200 (range, 150–261) pg/ml and by the end of the third year is 156 (range, 111–202) pg/ml. There needs to be a plasma level of etonogestrol of at least 90 pg/ml to suppress ovulation.

So why did this woman become pregnant? She was not overweight and had no history of use of enzyme-inducing drugs that could have predisposed her to ovulation. The fact that the residual content and calculated release rate of hormone were within the expected range would also tend to exclude extra rapid or slow metabolism of the hormone. Her plasma level of etonogestrel was 105 pg/ml, which is below the lower end of the range for the end of the third year of use but still higher than the level required to suppress ovulation. In vitro studies have shown that sertraline is a weak inhibitor of cytochrome P245, an enzyme involved in the elimination of Implanon. Sertraline, while the patient was taking it, would therefore have tended to increase the plasma level of etonogestrel, albeit weakly. With Norplant®, another progestogen-only subdermal implant, there have been pregnancies reported in the final years of the implant cycle. Perhaps for our patient an etonogestrel level of 105 pg/ml was insufficient to suppress ovulation, which had been prevented from occurring while she was taking sertraline by the small increase this drug produced in the plasma concentration? The product characteristics for Implanon state that no specific interaction studies have been done and so could an interaction have been responsible for ovulation?

The other interesting aspect of this case is the extraterine nature of the pregnancy. There were no predisposing factors for this, namely no previous pelvic...
inflammation, a negative chlamydia screen, and no abnormalities detected at the woman’s previous laparoscopy. One can only postulate that once ovulation occurred, the same mechanism that is known to predispose to ectopic pregnancy with oral progestogen-only contraception was responsible in this case also. Only one certain case of an ectopic pregnancy due to genuine failure of Implanon has been recorded in the literature, and interestingly the woman in that case had also had regular periods since implantation.2

Ectopic pregnancy is a potentially life-threatening condition, and the initial reports concerning the efficacy of Implanon could lull medical staff into a false sense of security that pregnancy – let alone an ectopic pregnancy – is impossible. This case illustrates the danger inherent in this way of thinking. It also highlights the need for further study of possible interactions between Implanon and other drugs.

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References
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