Ectopic Pregnancy After Removal of Levonorgestrel Implants: a Review of Two Case Series in a Resource Low-setting in Sub-Saharan Africa

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\section*{ABSTRACT}

\textbf{Background:} Contraception has been practice in the last few decades in order to prevent unwanted pregnancies and to safe women from criminal abortions and its complications. \textbf{Case presentation:} We report 2 cases of ectopic pregnancies diagnosed at 8 and 7 weeks of amenorrhea after the removal of levonorgestrel – containing implants in two females 28 and 32 years old respectively. The ectopic pregnancies occurred between 4-6 weeks following the removal of the implants. The patients were both manged with laparoscopy in Douala general hospital. \textbf{Conclusion:} Due to the limited data on the relationship between progestin implants and ectopic pregnancy, the authors advise that, after removal of the implants patients should not have unprotected sexual intercourse for about three months so as to allow ciliary functions to return to normal.

\textbf{Keywords:} Ectopic pregnancy, levonorgestrel, progesterone, laparoscopy, contraception, case report

\section{INTRODUCTION}

Criminal and elective termination of unwanted pregnancies remained a major public health problem in most developing countries as it increases the maternal mortality rate (MMR)\textsuperscript{(1)} Contraception has been practice in the last few decades in order to prevent unwanted pregnancies and to safe women from criminal abortions and its complications thereby decreasing maternal mortality\textsuperscript{(1,2)}. The levonorgestrel (LNG)-releasing subdermal implant is widely used in sub-Saharan Africa. After insertion, the implant may remain in place for up to 5 years during which LNG is released from the implant initially at 100 μg/day that later becomes stable maintaining a relatively stable daily drug concentration\textsuperscript{(3)}. Prolonged exposure to LNG in implants for a long period of time may lead to mucosal damage and decreased ciliary motility\textsuperscript{(4)}. Several original research and case reports have been published on the relationship between LNG as emergency contraception and ectopic pregnancy (EP)\textsuperscript{(1,5,6)}. A recent systematic review in 2015

showed EP is more common if LNG containing implants is used compared to implants containing other hormones\textsuperscript{4}. In this article the authors describes 2 cases of ectopic pregnancies diagnosed at 8 and 7 weeks of amenorrhea after the removal of levonorgestrel (LNG) – containing implants. The pregnancies occurred between 4 - 6 weeks following the removal of implants.

2. CASE REPORT

Case N° 1
Madame X is a 28 year old Cameroonian gravida 3 para 2 who presented at the gynecological unit of the Douala general hospital (DGH) with a history of spotted vaginal bleeding and lower abdominal pains on an amenorrhea of 8 weeks. In the past, she had placed Levonorgestrel (LNG) implant for the past 4 years as a means of contraception which was removed 4 weeks before the onset of menstruation that preceded the EUP. On physical examination at entry, she was haemodynamically stable, vaginal examination showed, a right adnexa mass and the uterus slightly increased in size, no bleeding. Transvaginal ultrasound showed an empty uterine cavity, a right ampulla gestational sac with cardiac activity and minimal haemoperitoneum. Serum beta human chorionic gonadotrophins (β-HCG) levels were elevated at 5700mIU/ml. An emergency laparoscopy was done which identified a right voluminous haematosalpinx measuring 50mm x 40mm and haemoperitoneum of 150cc. The corpus luteum was on the same side as the EP. There was no stigmata of infection or endometriosis capable of justifying the ectopic pregnancy. Total salpingectomy was done. The post-operative period was uneventful. Infectious salpingostomy was done. Histological analysis of the operative sample showed presence of chorionic villi. The post-operative period was uneventful. Intrauterine pregnancy and subsequently delivered at term.

Case N°2
Madame Y is a 32 year old Cameroonian gravida 4 para 3 who presented at the Gynecological service of the DGH for right iliac fossa pain and spotted vaginal bleeding on an amenorrhea of 7 weeks corresponding to her last menstrual period. In the past, she had had LNG implant for 3 years which she removed 5 weeks prior to the onset of menstruation. On physical examination at entry, she was haemodynamically stable, vaginal examination showed, a left adnexa mass, normal uterine volume, spotted vaginal bleeding. Transvaginal ultrasound showed an empty uterine cavity and a left ampulla gestational sac with cardiac activity; serum β-HCG levels were elevated at 28000mIU/mL. Emergency laparoscopy identified an unruptured left tubal ectopic pregnancy. The corpus luteum was on the same side as the ectopic pregnancy. The contralateral adnexa was normal and there was no stigmata of infection or endometriosis which could justify the ectopic pregnancy. A conservative linear salpingostomy was done. Histological analysis of the operative sample showed presence of chorionic villi. The post-operative period was uneventful. Infectious screen was normal (cervical smear for chlamydia and mycoplasma were negative). After informed consent was gotten on allowing a time lapse of 3 month before desiring pregnancy, we placed an intra-uterine device (IUD) containing copper. It was removed after 3 months on demand and 4 months later the patient had an intra-uterine pregnancy and subsequently delivered at term.

3. DISCUSSION

An ectopic pregnancy is a pregnancy where the blastocysts implants and develops out of the endometrial cavity\textsuperscript{7}. The incidence of EP varies with the population, but it has been estimated to account for 1-2\% of all reported pregnancies\textsuperscript{8,9}. Recent case control studies have identified the following factors to be associated with the development of EP: age, multiparty, prior ectopic pregnancy, use of intrauterine device, tubal damage, tubal surgery, smoking, failed emergency contraception and failed oral contraceptives\textsuperscript{7,9,10}. In our series presented no infection was identified after a complete workup and intraoperative laparoscopy showed no sequence of infection as the tubes were normal. Many cases of EP in the course of emergency contraception (EC) with levonorgestrel have been published in recent literature\textsuperscript{1,5}. The possible relationship between EC and EP is due to the high dose of progesterone on ciliary function. LNG taken at once in the EC has a high dose progesterone (750µg) that causes ciliary dysfunction\textsuperscript{11}. Our two indexed cases of EUP that we reported are not in a context of utilisation of emergency contraception, but occurred in a relatively short time lapse of 4-6 weeks after removal of LNG.
implants. Association between low progesterone level and EP have long been described, low serum progesterone influences the oviduct electrophysiological characteristics leading to poor ovum transfer, low probability of pro-uterine propagation of the activity at the fimbria end of the tube; high frequency but low number of electrical bursts, reflecting possible weak propulsive force and consequently increasing the rate of ovum retention and ectopic pregnancy\(^\text{[12,13]}\). The long term use of the progestin containing implant also causes myorelaxation and further increasing the rate of EP\(^\text{[4]}\). This together with multiparty are plausible mechanisms for the development of EP in our indexed cases.

4. **CONCLUSION**

Although there is limited data on the relationship between ectopic pregnancy and LNG implants. After removal of LNG implants, patient should be advised not to have unprotected sexual intercourse for about three months so as to allow the myorelaxant effects of progestin to finish. Furthermore, patients with a positive pregnancy test after removal of LNG implants should be monitored closely in order to rule out the possibility of an ectopic pregnancy. We therefore recommend that a case control study be carryout to establish the association between LNG implants and EP.

**REFERENCES**