Medical Management of Ectopic Gestation Following a Failed Bilateral Tubal Ligation.

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Summary

The objective of this paper is to emphasize that ectopic pregnancy can occasionally occur after a previous bilateral tubal ligation. Affected women may be reluctant to undergo a repeat surgery and medical management is an acceptable approach in suitable cases. The case was a40-Year-old G5P4+0 (3A) woman who presented to gynaecology clinic with 7-weeks history of amenorrhoea and 1day history of bleeding from the vagina. She has had two previous caesarean section and bilateral tubal ligation during her last confinement in 2018. Ectopic pregnancy was confirmed, and she was medically managed with methotrexate.Pregnancy after bilateral tubal ligation is rare and when it occurs are rarely ectopic pregnancy. Medical management can be offered to suitable patients where there is facility for follow-up.

Key words: Methotrexate, Ectopic pregnancy, Bilateral tubal ligation, Serum Beta HCG, Caesarean Section

Introduction:

Bilateral tubal ligation (BTL) is a form of permanent contraceptive technique commonly recommended to women with completed family size. Though with declining rates over the past 20 years, it is the commonest contraceptive used worldwide, accounting for 23.7% of women using contraceptive, but with about the least uptake in Sub-Saharan Africa[1]. Newer methods of sterilization have evolved over the years with a shift towards minimally invasive techniques, however in Nigeria, mini-laparotomy and caesarean BTL are the common methods using the Pomeroy's technique[2,3].

As effective as it is, it has a failure rate of 0.5%[4-6]A failure rate of 0.1-0.8% in the first year after tubal sterilization has also been reported.[7]. Ectopic pregnancy could be managed surgically, by medical means or even by expectant management; all these have specific criteria[4,8]. If pregnancy occurs following tubal ligation, the risk of it being an ectopic is 12.5%[9]. In this report, we present medical management of ectopic pregnancy following a failed caesarean bilateral tubal ligation.

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Case Summary

Mrs O.E was a 40-Year-old G5P4+0 (3A) woman who presented to the gynaecology clinic on 6/11/2019with 7weeks history of amenorrhoea and 1day history of bleeding from the vagina. There was no passage of blood clot or vesicles, no dizziness or fainting attacks, no abdominal pain. She had performed urine pregnancy test on two different occasions before presenting, and both were positive.

In 2011 she conceived spontaneously and had induction of labour at gestational age of 40 weeks in a private hospital because of severe preeclampsia but she gave birth to a fresh stillborn baby. She had no puerperal problem.In 2012, she conceived spontaneously and presented to hospital with labour pain at gestational age of 39weeks and 1 day but the baby developed heart irregularities and she subsequently had emergency caesarean delivery of a live male neonate with birth weight of 3Kg. He is alive and well. In 2015, she conceived spontaneously again and received adequate antenatal care, initially scheduled to have trial of vaginal birth after caesarean section, but however had elective caesarean section at gestational age of 41weeks and 3 days because of 1previous caesarean section and postdatism and was delivered of a live female neonate with birthweight of 3.4Kg. Puerperium was uneventful and baby is alive and well.

In 2018, she conceived spontaneously, and booked for antenatal care at gestational age of 20 weeks and 4 days; She was counselled for permanent contraception at the time of delivery which she and her husband consented to. In October 2018, she was admitted at gestational age of 38-weeks and had elective caesarean section with bilateral tubal ligation on account of 2 previous caesarean section and complete family size. The tissue specimens taken were sent for histology which showed tubular structures in keeping with the fallopian tube.

She was not a known hypertensive, diabetic, asthmatic or peptic ulcer disease patient. She had not

previously had blood transfusion. She neither smoked cigarette nor drank alcohol. She did not have any known drug allergy.

Clinical examination revealed a young woman, not pale, anicteric, afebrile, well hydrated with no pedal oedema. Her respiratory rate was 18/min, with clinically clear chest. Her pulse rate was 80/min, blood pressure: 120/70mmHg, the first and second heart sounds were heard with no added sounds. Her abdomen was full and moved with respiration, Pfannenstiel scar was noted. There were no areas of tenderness and no palpable mass; neither the uterus nor the intra-abdominal organs were palpable Vaginal examination showed a normal vulva and vagina. Cervix was firm, posterior and os closed. Uterus was not palpable by bimanual examination, adnexa were free, cervical motion tenderness test was negative and the pouch of Douglas was flat. There was minimal blood stain on gloved fingers. A diagnosis of threatened miscarriage to rule out ectopic gestation was made

Repeat pregnancy test was positive. Pelvic ultrasound done showed normal size uterus measuring 4.6 x 5.5 x 12.3cm, endometrium was 4mm and normal. Right ovary not seen separately from a 31 x 30 x 52 mm = 26cm^3 oval rounded vascular heterogeneous solid mass in the region of the right fallopian tube. Left ovary measured 24 x 15 x 16 mm = 3.3cm^3. Normal pouch of Douglas. The ultrasound diagnosis was right ectopic pregnancy, in view of a positive pregnancy test and a differential diagnosis of enlarged right ovary.

She had a serum beta human chorionic gonadotrophin (hCG) done which was 8,900 IU/L and this was repeated in72 hours and found to be 8,874 IU/L. She was then counselled on medical management and was appropriately investigated. She had a Full Blood Count (FBC) and differentials (Haematocrit [HCT] 35.5%, White Blood Count [WBC] 5.6 X 10^3/ml, Neutrophils 60%, Lymphocytes 30%, Monophils 5.3%, Platelets[PLT] count 424 x 10^3/ml), Liver Function Tests (LFT)(Alanine transaminase [ALT] 14mmol/l, Aspartate aminotransferase [AST] 19mmol/l, Alkaline phosphatase [ALP] 65mmol/l, total protein 7.5g/l, Albumin 4.0g/l, Bilirubin 0.2mg/dl), Serum Electrolytes and Urea(Sodium 139mmol/l,Potassium 3.6mmol/l, Chloride 98mmol/l, Bicarbonate 24mmol/l , Urea 40mg/dl) done and these were also within normal limit.

She was planned for single agent intramuscular Methotrexate at a dose of 50mg/ Body Surface area (BSA). She had pre-chemotherapy medication with two intravenous doses each of Ranitidine 50mg, Ondansetron 8mg and Dexamethasone 8mg given slowly 8 hours apart on each day of chemotherapy. She always had 500ml each

Table 1: Serial quantification of Serum beta human chorionic gonadotrophin (βhCG).

Date	Serum βhCG level (IU/L)	% drop in βhCG level	Intervention
08/11/2019 (PrePresentation)	8874	--	Nil
12/11/2019(96hrs later)	5969	32.74 (over 4 days)	1st course
18/11/2019	2522	57.75	2nd course
25/11/2019	338.7	86.57	3rdcourse
09/12/2019	16.6	95.10	4th course
17/01/2020	0.2	98.80	No morechemotherapy

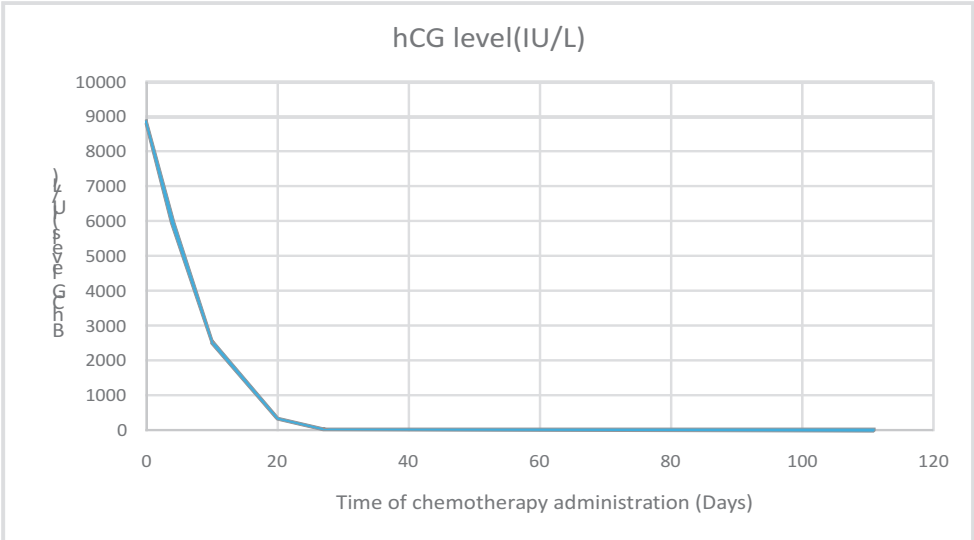

Figure 1: A graph showing the relationship between the serum beta hCG (vertical axis) and Time (in days) of administration of chemotherapy (Methotrexate).

of normal saline and 4.3% dextrose saline given over 1-2 hours before commencing the premedication.The intramuscular methotrexate was then administered about 15-30 minutes after the second doses of premedication.

She was managed on an out-patient basis with the patient admitted in the ward as a day case on the day of chemotherapy and then discharged home about half an hour post chemotherapy. With a BSA of 1.62, she received 85mg of methotrexate. About 96 hours after the first dose, there was approximately 57.75% decline in the level of serum hCG from 5969 to 2522 IU/L.

She was scheduled for weekly serum hCG assay and for repeat weekly methotrexate until the serum beta hCG becomes undetectable. Prior to each course of chemotherapy, she had repeat FBC + differentials, LFTs and Serum E&Udone,and they were all within normal limit. She came weekly for the second and third doses but defaulted because of financial reasons for a period of two weeks before the fourth dose. The serum level of beta hCG dropped precipitously after each dose of methotrexate. After the second dose, 86.57% fall, 95.10% decline after the third dose and 98.80% fall after the fourth dose at which point the hCG level had returned to normal level. She did not develop any side effect of methotrexate throughout the period of treatment and follow up.

She was counselled on the need for alternative contraceptive method and the option of vasectomy for her husband. Additionally, she was counselled on the risk of future ectopic pregnancy and the need to present early after missing her period. She was then given a 3-months clinic appointment for follow-up.

Discussion

Tubal ligation is a common surgical procedure aimed at permanently blocking the fallopian tubes to prevent spermatozoa from reaching an ovum for fertilization. It involves the tubes being cut and tied, cauterized, blocked with rings or clips and intratubal injection or insertion of sclerosants or devices[8]. It is commonly done by mini-laparotomy or laparoscopically but recently through hysteroscopic methods[10,11]. It is an effective method of contraception, but method failure has been reported as low as 7 pregnancies per 1000 procedures[12-14] The failure rates vary among the different methods and higher failure rates has been documented amongst BTL done at caesarean section[15].

Pregnancy occurring after BTL can be emotionally disturbing to the woman and are mostlyintrauterine[16,17]. In 12.5% of cases, these could be ectopic pregnancy and heterotopic pregnancy following BTL has also been reported[8]. The occurrence of ectopic pregnancy after BTL may be due to spontaneous tubal recanalization or the formation of tubo-peritoneal fistula[9,16]. An ectopic pregnancy is termed the implantation of a fertilized ova outside the endometrial lining of the uterine cavity and it is a life-threatening event. It's morbidity and mortality increase when patients present with ruptured ectopic pregnancy. Depending on the presentation, ectopic pregnancy could be managed conservatively, medically or surgically. Mrs O.E presented with features suggestive of unruptured ectopic pregnancy, so she was considered suitable for medical management.

Medical management of ectopic gestation often involves the use of systemic methotrexate[8].The benefits of the medical management are that it potentially causes less tubal damage, avoids the risk of morbidity associated with surgery and anaesthesia and is cost-effective which makes it more relevant in low resource countries. It however has its own draw backs from the side effects of the medications given and that it may require prolonged hospitalization but improvements in the protocol over the years have made it possible for single dose outpatienttherapy[18].

The patient must satisfy the criteria for medical management of ectopic pregnancy which include being clinically stable with no significant pain, having an unruptured tubal ectopic with adnexal mass smaller than 35mm with no visible heartbeat, and serum hCG level less than 1,500IU/L, ultrasound confirmation of absent intrauterine gestation and a patient who was willing to return for follow up[8].Although the patient in question did not meet all the above criteria, in view of her haemodynamic stability, ultrasound findings (including lack of a fetal heart tone and absence of evidence of rupture),and willingness to come for follow-up, even though the serum beta hCG level was high (8874 IU/L) and the size of the ectopic sac could not be ascertained since it could not be delineated from the right ovary, medical management was still offered to this patient.

The patient received intramuscular Methotrexate at a dose of 50mg/ Body Surface area (BSA). With a BSA of 1.62, she received 85mg of methotrexate. About 96 hours after the first dose, there was approximately 57.75% decline in the level of serum hCG. After the second dose, 86.57% fall, 95.10% decline after the third dose and 98.80% fall after the fourth dose at which point the hCG level had returned to normal level. Although, there is no consensus on whether to use a single dose or multiple courses of chemotherapy, the multiple course regimen has been documented to be associated with greater success and it was adopted in the management of Mrs. O.E[18].

The initial intention was to perform weekly serum hCG level assessment and administer intramuscular Methotrexate weekly but because of financial constraint, she could not catch up with that pace. However, because of good and on-going counselling the patient was able to continue the

management to this satisfactory point without defaulting.

Side effects of methotrexate include blood disorders (bone marrow suppression), liver damage, pulmonary toxicity; gastrointestinal disturbances such as stomatitis and diarrhoea renal failure, skin reactions, alopecia, osteoporosis, arthralgia, myalgia and ocular irritation[18]. However, throughout the period of treatment, the patient did not have any of these symptoms or signs and the pre-chemotherapy investigations were within normal limit. She was hydrated and had pre-chemotherapy medications with Ranitidine, Ondansetron and Dexamethasone. The aim of this was to reduce to the barest minimum the possible side effects of the chemotherapeutic agent used.

She was counselled on the need for alternative contraceptive method and she has chosen to use combined oral contraceptive pills for now. Though she was counselled on the need for long acting reversible contraception, but because of her previous unpalatable experience of excessive bleeding with injectables and abnormal vaginal discharge with copper-containing intrauterine devices she did not want them. She wanted some more time to think on implants though she was afraid of weight again and abnormal menses as her friends narrated their experiences to her. Another possible option is to counsel her husband for vasectomy, however the cultural acceptability is low in this environment.

In conclusion, no contraceptive method is 100% safe. Where failure occurs and pregnancy results, early diagnosis and prompt management is key so as to reduce the possible morbidity and mortality that may ensue, and where medical management could replace surgical care, clinician should carefully select the patient and apply medical rather than operative care, especially when it may not significantly improve the patient's outcome.

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